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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,428	03/19/2001	Magnus Hook	P06668US03/BAS	6490

881 7590 08/10/2005

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,428	HOOK ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1, 3-5, 7, 10, 12-14,15-22,26- 30 and 33-34* is/are pending in the application.

4a) Of the above claim(s) *15-22,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 7, 10, 12-14, 23, 26, 29, 30 and 33-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment

1. Applicant's amendment filed on 5/05/05 is acknowledged.

Status of Claims

2. Claims 2, 6, 8-9, 11, 24-25, 31 and 32 are canceled.

Claims 1, 23, 29 and 34 have been amended.

Claims 1, 3-5, 7, 10, 12-14, 23, 26, 29, 30 and 33-34 are under examination as an elected invention.

Claims 15-22 and 27-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

3. Information Disclosure Statement (second supplement) filed on 2/2/05 is acknowledged and a signed copy is attached to this Office action.

Claim Objection withdrawn

4. In view of amendment to the claim 34, the claim objection is withdrawn.

Claim Rejections - 35 USC 112 withdrawn

5. In view of amendment to the claim 1, the rejection under 35 U.S.C. 112, second paragraph is withdrawn.

Claim Rejections - 35 USC 102 withdrawn

6. In view of cancellation of claims, amendment to the claims, arguments of record along with the Declaration of record, 5/5/05, Dr. J. Patti, (see Para # 9 and 10), the rejection under 35 U.S.C. 102(b) as being anticipated by Schiotz et al Acta.Pathol Microbiol Scand 1979, 87(6) 329-36 is withdrawn.

7. In view of cancellation of claims, amendment to the claims, arguments of record, the rejection under 35 U.S.C. 102(b) as being anticipated by Espersen et al Acta.Pathol Microbiol Scand 1981, 89:253-260 is withdrawn.

8. In view of cancellation of claims, amendment to the claims, arguments of record, the rejection under 35 U.S.C. 102(b) as being anticipated by Patti et al (Journal of Biological Chemistry. May 1995, Vol, 270. No 20, pages 12005-12011) is withdrawn.

9. In view of cancellation of claims, amendment to the claims, arguments of record along with the Declaration of record, the rejection under 35 U.S.C. 102(b) as being anticipated by Patti et al (Journal of Biological Chemistry. May 1992, Vol, 267. No 7, pages 4764-4772) is withdrawn.

Double Patenting Rejections maintained

10. The rejections made under obviousness-type double patenting and under 35 U.S.C. 103(a) are maintained for the same reasons as set forth in the previous Office action.

Claims 1, 3-14, 23, 26, 29 and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 09/813,820. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims of the instant application and those of copending Application No. 09/813,820 are drawn to antibodies that bind to collagen binding protein and prevent S.aureus infection. Monoclonal and polyclonal antibodies to SEQ.ID.NO: 4 of the copending application bind to amino acids 61-343 of the full length CNA protein and therefore it is obvious that these antibodies bind to CNA 19 peptide of the present application that contains amino acids 151-318 of the full length CNA protein and is within the collagen binding region. Further, the antibodies of the copending application are monoclonal and polyclonal antibodies and are used as pharmaceutical composition to treat S.aureus infection. Therefore, antibodies that bind to CNA 19 peptide read on the antibodies of co-pending application. Antibodies that bind to collagen binding region, amino acid 61-343 would also bind to a smaller CNA 19 peptide that contains amino acids 151-318. The co-pending application teaches monoclonal and polyclonal antibodies to SEQ.ID.NO: 4 inhibit the bacterial adhesion to collagen and thereby preventing S.aureus infection. However, the diagnostic kits comprising

these antibodies are not taught in the copending application. An artisan of ordinary skill would have been motivated in applying the art disclosed by the prior art because these antibodies specifically bind to S.aureus CNA peptide and kits that contain the antibodies which recognize the S.aureus infection would help in diagnosing S.aureus infection conveniently and do not

require trained technical support since it comes with instructions to use. Kits were well known in the art for testing or diagnosing varieties of diseases. Instructions are printed matter which have been long been held to distinguish a claimed structure over the prior art only where the printed matter functions in cooperation with the structure. Here there is no such functional cooperation between the printed instructions and the kit's structural components. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to keep the antibodies as disclosed by the prior art in the form of a compact kit since kits are easy to transport and convenient to work in places (economically under developed countries) with less facilities.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 1, 3-14, 23, 26, 29 and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S.Patent 6,288,214. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims of the instant application and those of Patent are drawn to antibodies that bind to collagen binding protein and prevent S.aureus infection. The disclosed antibodies to SEQ.ID.NO: 6 of the Patent bind to amino acids 30-531 of the full length collagen binding protein, CNA and therefore it is obvious that these antibodies bind to CNA 19 peptide of the present application that contains amino acids 151-318 of the full length CNA protein and is within the collagen binding region. Further, the antibodies disclosed in the patent are monoclonal and polyclonal antibodies and are used as pharmaceutical composition to treat S.aureus infection. Therefore, the instant claims drawn to antibodies that bind to CNA 19 read on the prior art antibodies that bind to collagen binding region (amino acid 30-531) would also bind to a smaller CNA 19 (amino acids 151-318) peptide. The prior art teaches monoclonal and polyclonal antibodies to SEQ.ID.NO: 6 inhibit the bacterial adhesion to collagen and thereby preventing S.aureus infection. However, the prior art does not teach diagnostic kits comprising these antibodies.

An artisan of ordinary skill would have been motivated in applying the art disclosed by the prior art because these antibodies specifically bind to S.aureus CNA peptide and would be useful in diagnosing S.aureus infection. Kits containing these antibodies are convenient to work and do not require trained technical support since it comes with instructions to use. Kits were well known in the art for testing or diagnosing varieties of diseases. Instructions are printed matter which have been long been held to distinguish a claimed structure over the prior art only where the printed matter functions in cooperation with the structure. Here there is no such functional cooperation between the printed instructions and the kit's structural components. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to keep the antibodies as disclosed by the prior art in the form of a compact kit since kits are easy to transport and convenient to work in places with less facilities.

12. Claims 1, 3-14, 23, 26, 29 and 33 are also rejected under 35 U.S.C. 103(a) as being obvious over U.S.Patent 6,288,214

The applied reference has a common inventor (i.e., Hook. M) with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37

CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The prior art teaches antibodies to SEQ.ID.NO: 6. These antibodies bind to amino acids 30-531 of the full length CNA protein and therefore it is obvious that these antibodies bind to CNA 19 peptide that contains amino acids 151-318 of the full length CNA protein and prevent S.aureus infection. Further, the antibodies taught by the prior art are monoclonal and polyclonal antibodies and are used as pharmaceutical composition to treat S.aureus infection. The prior art teaches monoclonal and polyclonal antibodies that bind to SEQ.ID.NO: 6, which inhibit the bacterial adhesion to collagen. The prior art monoclonal and polyclonal antibodies inhibit the bacterial adhesion to collagen, i.e., antibody capable of displacing S.aureus to collagen (see abstract, figures 5-7 and columns 15-19 and claims). Further the prior art teaches antibodies prevent S.aureus infection (i.e., antibody capable of displacing S.aureus to collagen, see figures 7- 8) and other related bacterial colonies (column 4, lines 45-50). Therefore, the disclosed antibodies are cross-reactive to S.epidermidis. The prior art also teaches diagnostic kits comprising the antibodies (column 26). Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the antibodies of the prior art because the antibodies disclosed specifically bind to collagen binding region (amino acids 30-531) would also bind to smaller CNA peptide that contains amino acids 151-318 and is within the collagen binding region. An artisan of ordinary skill would have been motivated to use the antibodies disclosed because it would have helped in diagnosing and treating S.aureus or S.epidermidis infections. The claimed invention is a prima facie obvious in view of Hook et al absent any convincing to the contrary.

Applicants' arguments filed on 8/23/04, have been fully considered but they are not deemed to be persuasive.

Applicant states that an isolated antibody which recognizes the CNA 19 region, amino acids 151-318 of the collagen binding domain from the S. aureus CNA protein is cross reactive to S.epidermidis and it is an unexpected beneficial result as shown in the accompanying the Declaration provided by Dr Magnus Hook. Further applicant explains the binding properties of these bacteria are different. Applicant states that the binding protein of *S.epidermidis* GehD Lipase enzyme differs from CNA19. However, the claimed antibody is an unexpected result over the prior art. Finally applicant states that the examiner is totally inaccurate and has no basis in stating that antibodies bind to the full length protein binds to the CNA19 region, amino acids 151-318 of the collagen binding domain. No prior art antibodies exhibited the unexpected cross- reactivity of the antibodies to the CNA -19 region. Accordingly, these references would not anticipate or render the present claims obvious.

The examiner carefully reviewed the declaration submitted by Dr Magnus Hook and understands and respects his contribution to the art. However, the claims are drawn to an antibody, which cross-reacts to S.epidermidis and S.aureus. The claims do not recite the structural differences of the protein to which the antibody binds as discussed by the applicant. The claims do not set forth the binding regions of the cross-reactive antibody to which S.epidermidis and S.aureus bind. Please note, none of the claims recite that the claimed antibody recognizes GehD Lipase enzyme on S.epidermidis and the GehD recognized by the

antibody to CNA19 has a circular dichrosim spectra that differs from that of CNA. Applicant keeps on arguing about the limitations such as structural differences of proteins, which are not set forth in the claims.
Further, applicant (Declaration) provided Appendix A and B, references from Infection and Immunity 49 (3): 700-708 (Appendix A) and J. Biol. Chem. 277(45): 43017-43023 (November 8, 2002) and Appendix B (J. Biol. Chem. 277(45): 43017-43023) to show the differences between S. aureus and S. epidermidis surface antigens.

The examiner has reviewed the article Appendix A and understands that the clumping factor component could be eluted from S.aureus cell wall, whole cells and extra cellular products by affinity chromatography on fibrinogen linked Sepharose 4B but not from sonicated preparations of S.epidermidis. The components bind to human fibrinogen and inhibit the fibrinogen induced clumping factor. Appendix A specifically teaches the fibrinogen binding proteins (clumping factor is specific for S. aureus) of S.aureus. However, the claimed invention is drawn to collagen binding proteins. In addition, it appears that not only S.epidermidis but also other staphylococcal L-forms do not contain clumping factor component (fibrinogen binding protein). Therefore, the reference does not teach cross-reactive antibodies to surface antigens of S.aureus and S.epidermidis.

The examiner would like bring applicant's attention to some of the art which show the cross reaction between S.epidermidis and S.aureus using antibody/antigen reference system by Schiotz et al Acta.Pathol Microbiol Scand 1979, 87(6) 329-36 and Espersen et al (Acta.Pathol Microbiol Scand 1981, 89:253-260).

Schiotz et al disclose cross reactive rabbit antibody raised against 55 antigens found in a mixture of sonicated preparations of S.aureus. Twelve of S.aureus antigens cross-reacted with the four S.epidermidis biotypes (seeTable 1 and Figure 3 A and B) using said polyclonal antisera (see under 102 (b) rejection). The polyclonal antibodies raised against sonicated preparations of S.aureus includes collagen adhesion surface antigen. Therefore, the disclosed antibodies read on the claimed cross-reactive antibody.

In addition, Espersen et al (Acta.Pathol Microbiol Scand 1981, 89:253-260) disclose cross reactive rabbit antibody raised against 43 antigens found in a mixture of sonicated preparations of S.epidermidis. Fourteen of the S.epidermidis antigens cross-reacted with antigens of all S.aureus strains (see Table 3, and abstract). Thus these references teach antibodies to surface antigens of S.aureus cross-reacted with surface antigens of S.epidermidis and vice versa.

With respect to Bowden et al 2002 Appendix B (J. Biol. Chem. 277(45): 43017-43023), the examiner reviewed the Appendix B and understands that antibodies to CNA19 appear to bind to the extra cellular lipase enzyme originally found in S.epidermidis 9 as a collagen binding protein. The mature GehD circular dichroism spectra differs from that of CNA but strongly resembles that of a mammalian alpha 1 integrand I domain indicating that they have similar secondary structures. This suggests GehD is bifunctional molecule acting not only as lipase but also as a cell surface –associated collagen adhesin (see abstract).

The examiner also reviewed the art, for example Longshaw et al Microbiology 2000, 146; 1419-1427 and understands that the sequence homology of mature lipase (binds to collagen I, II and IV) GehD between S.epidermidis and S.aureus is quite striking (see Figure 4 and Table 2) and the mature lipases particularly showed high degree of conservation between S.aureus and S.epidermidis (see figure 4). Thus the reference teaches high degree of conservation between mature lipases of S.aureus and S.epidermidis and suggests they might have similar secondary structures (collagen adhesion). This indicates that these two bacteria

S.aureus and S.epidermidis have common secondary conservative antigens present in collagen.

Thus, the art discloses cross-reactive antibodies between S.aureus and S.epidermidis. Further, the prior art cited by the examiner U.S.Patent 6,288,214 clearly suggests preventing bacterial adhesion using collagen specific products such as antibodies (column 43, lines 50-53, column 32, lines 40-46 and abstract). Therefore, the rejections of record are proper for this broadly claimed invention.

Applicants' arguments filed on 5/5/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that the cited application, 09/813,820 is in fact a pending divisional application of the application, which issued as U.S. Pat. No. 6,288,214, so all of these references have equivalent disclosures, namely they relate to the full collagen binding protein and antibodies thereto, and to an antibody raised to the M55 region of the collagen binding protein, and do not disclose or suggest the present monoclonal antibody because the monoclonal antibodies as claimed are epitope specific and gave an excellent results in achieving protection and it is extremely unlikely that monoclonal antibodies raised against greater region (amino-acid 30-531) would be able to recognize the specific epitope within a given region. The cross reactivity of the antibodies is unexpected. In addition, Applicant provided a Declaration by one of the inventors Dr Joseph Patti.

The examiner disagrees with the applicant because applicant has not shown any evidence that the claimed monoclonal antibody to 151-318 is not obvious over an antibody that binds to full length CNA (U.S.Patent 6,288,214) protein and antibody that bind to region 61-343. The examiner reviewed the Declaration provided by Dr Patti (dated 5/5/05) carefully and also noted the contents. However, the evidence submitted is insufficient to overcome the rejection of record as discussed in paragraph # 15.

Claim Rejections - 35 USC 102 maintained

13. The rejection of claims 1, 3-5, 7, 10, 12-14, 23, 26, 29, 30 and 33-34 under 35 U.S.C. 102(e) as being anticipated by Hook et al 2001 U.S.Patent 6,288,214 is maintained as set forth in the previous office action.

The disclosed antibodies to SEQ.ID.NO: 6 of the Patent bind to amino acids 30-531 of the full length CNA protein. Therefore, these antibodies bind to CNA 19 peptide of the present application that contains amino acids 151-318 of the full-length CNA protein and prevent *S.aureus* infection. The antibodies disclosed in the patent are polyclonal and monoclonal antibodies and are used as pharmaceutical composition to treat *S.aureus* infection (see abstract, figures 5-7 and columns 15-19). Further the prior art discloses antibodies that prevent *S.aureus* infection (i.e., antibody capable of displacing *S.aureus* to collagen, (see figures 7- 8) and other related bacterial colonies (column 4, lines 45-50). Therefore, the disclosed antibodies are cross-reactive to *S.epidermidis*. The prior art also discloses diagnostic kits comprising the antibodies (column 26). Since the Office does not have the facilities for examining and comparing applicants' product and method of use with the product and method of use of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430. The prior art anticipated the claimed invention.

14. The rejection of claims 1, 3-5, 7, 10, 12-14, 23, 26, 29, 30 and 33-34 under 35 U.S.C. 102(b) as being anticipated by Hook et al WO97/43314 20 November 1997 (20.11.1997) is maintained as set forth in the previous office action.

Hook et al disclose the 19,000 M collagen-binding domain from Staphylococcus aureus, also known as CNA-19. The 19kD protein contains the 168 amino acid long segments, specifically amino acids 151-318 of the protein that has appreciable collagen binding activity (page 3). Hook et al., disclose the preparation of immunological compositions such as anti-collagen binding protein (CBP) antibodies for diagnostic and therapeutic methods for detection and treatment of infections caused by S. aureus s (page 16). The antibody compositions disclosed bind to altered proteins, specific to native collagen and synthetically mutated CBP with domain specific epitopes within the CBPs (page 16). The antibodies have been shown to inhibit collagen binding to CBP and *S.aureus* binding to extra cellular matrix by both in vitro and in vivo (page 26 and claims) assays. Hence the antibodies displace *S.aureus* bound to collagen. The antibodies are monoclonal (page 26 and claims) antibodies and interact with collagen binding domain of a staphylococcal cna gene product (claim 1). Therefore, the antibodies could cross react with other staphylococcal cna gene products such as *S.epidermidis*. The vaccine formulation are useful against streptococcal and staphylococcal infection (page 29). The therapeutic and diagnostic kits comprising CBP compositions include antibodies and labels (page 37-39). The administration of antibodies reactive with CBP to at-risk subjects will be effective for prophylaxis of and in the case of infected subjects for therapy of bacterial infections (page 17). Preferred animals to receive treatment include mammals and particularly humans (page 18). Also taught were immunoassays for detection in ELISA plates, dot blots and western

analysis (page 20). Exemplary samples include clinical samples of blood and serum (page 21). Also taught are methods for inhibiting bacterial adhesion to collagen (page 22). Therefore, in the absence of evidence to the contrary the disclosed antibodies against CNA read on the claimed invention. Since the Office does not have the facilities for examining and comparing applicants' product and method of use with the product and method of use of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430. The prior art anticipated the claimed invention.

Applicants' arguments filed on 5/5/05 have been fully considered but they are not deemed to be persuasive.

15. Applicant states that the U.S.Patent 6,288,214 and WO97/43314 do not disclose or suggest the claimed invention because the monoclonal antibodies as claimed are epitope specific and gave an excellent results in achieving protection and it is extremely unlikely that monoclonal antibodies raised against greater region (amino-acid 30-531) would be able to recognize the specific epitope within a given region. The cross reactivity of the antibodies is unexpected. In addition, Applicant provided a Declaration by one of the inventors Dr Joseph Patti.

The WO97/43314 reference is a statutory bar under 35 U.S.C. 102(b) and thus cannot be overcome by an affidavit or declaration under 37 CFR 1.131.

With respect to reference U.S.Patent 6,288,214 the examiner reviewed the Declaration provided by Dr Patti (dated 5/5/05) carefully and also noted the contents. However, the evidence submitted is insufficient to overcome the rejection of record for the following reasons:

(1) The Declaration states that Dr. Joseph M. Patti is one of the inventors of the above-identified patent application and is a co-inventor for many Patents including U.S. Pat. No. 6,288,214. However, the declaration does not provide any evidence how and why the antibodies in the Patent would not recognize the binding region at amino acids 151-318 since the claimed as well as disclosed antibodies prevent *S.aureus* infection and also inhibit the bacterial adhesion to collagen.

(2) It states that the claimed isolated monoclonal antibody was not at all expected, as the antibody recognizing CNA19 of *S. aureus* would recognize epitopes from S. *epidermidis* (gram negative) and explains the differences between these bacteria. However, cross-reactive monoclonal antibodies have not been distinguished (for example: specific hybridoma cell line) from that of antibodies to full length CNA. Therefore, in the absence of evidence to the contrary the disclosed antibodies have the same function.

(3) The declaration states that the ability of monoclonal antibody to CNA19, displacing S. aureus cells adhering to collagen were one of the most remarkable and unexpected properties of the claimed antibody. However, the declaration failed to distinguish the claimed antibody from the other antibodies that bind to the CNA 19 protein since the prior art antibodies also inhibited the *S.aureus* infection by preventing the bacterial adhesion to collagen.

(4) The declaration indicates that none of the references disclosed or suggested the particular monoclonal antibody capable of displacing *S. aureus* to collagen. However, there is no evidence that the prior art monoclonal antibody and the claimed antibody are different to each other. Therefore, in the absence of evidence to the contrary the disclosed antibody has the same property and function of claimed "particular monoclonal antibody".

(5) The declaration states that the Examiner is incorrect and untrue in stating that the prior antibodies to the full CNA protein and to the M55 region (SEQ ID NO: 6 of U.S. Pat 6,288,214) would recognize the CNA19 region at amino acids 151-318 of the CNA protein, particularly in the case of very specific monoclonal antibodies for specific epitope within a given region. However, no specific epitope of the specific monoclonal antibody has been provided to support applicant's arguments. Therefore, antibodies that bind to 30-531 region would bind to 151-318 region because the antibodies have the same function in preventing *S.aureus* infection by preventing collagen adhesion. Applicant has not provided any data that monoclonal antibodies to CNA (aa30-531aa) would not bind to aa151-318aa of CNA when antibodies to full length CNA have been shown to confer protection against *S.aureus* infection.

(6) The declaration states that the protection against *S.epidermidis* varies with different classes (IgM versus IgG) antibody as shown by Iechiman, 1991 (abstract, exhibit A, Can J Microbiol. 1991 May; 37(5): 404-7) indicating uncertainty of protection. However, the exhibit does not provide evidence that the disclosed antibodies would not recognize the binding region of CNA19 as the monoclonal antibodies to full-length protein have been patented and confer protection against *S.aureus* infection by inhibiting collagen binding.

Additionally as applicants are aware that conformational dependent epitopes are important in recognizing the monoclonal antibody. Further it is not clear that the epitopes recognized by the claimed CNA mab and mAb with good inhibiting and displacing activities are located throughout the structure of CNA-151-318. Applicant's declaration does not indicate the differences between displacing mAb and the collagen binding inhibiting mab, Therefore, in the absence of evidence to the contrary, the prior art monoclonal antibodies that confer protection against *S.aureus* infection by inhibiting collagen-binding read on the claimed invention.

New Claim Rejections - 35 USC § 112 based on amendment

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 10, 13 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10 and 26 are rejected as being vague for the recitation of "isolated antisera " because claim 1 is drawn to monoclonal antibodies and the term "antisera" is used in the art for serum antibodies that are isolated from blood from an animal immunized with an antigen. Monoclonal antibodies are not isolated from antisera.

Claim 13 is rejected as being vague for the recitation of " means for detecting binding by than antibody". Does applicant intend to mean the claim to recite "means for detecting antibody binding?"

Remarks

16. No claims are allowed.

Relevant Prior Art

17. The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

Schiotz et al Acta.Pathol Microbiol Scand 1979, 87(6) 329-36 teach polyclonal antibody (Ref.Ab) preparation consisted of purified immunoglobulins, isolated from pooled rabbit antisera immunized with a mixture of sonicated preparations (containing 55 antigens) of S. aureus (see page 330, right column, last paragraph through page 331, left column first paragraph). All 12 antigens of the *S.aureus* cross-reacted with four biotypes of *S.epidermidis* (see Table 1, and figure 3A and B). The teaching of the prior art indicates that cell wall peptidoglycan is one of the cross-reactive antigens between gram positive and gram-negative bacteria.

Espersen et al Acta.Pathol Microbiol Scand 1981, 89:253-260 teach polyclonal antibody (Ref.Ab) preparation isolated from pooled rabbit antisera immunized with a mixture of sonicated preparations of *S.epidermidis*, said antibody is polyclonal, said antisera contains antibody. (see page 254, left column, third paragraph). Fourteen of the *S.epidermidis* antigens cross-reacted with antigens of all *S.aureus* strains (see Table 3, and abstract) using said antibody. The teaching of the prior art indicates that cross-reactive antigen is a cell wall peptidoglycan (see page 258, second paragraph) of the bacteria.

Patti et al Biochemistry. 1993 Oct 26; 32(42): 11428-35 teach the expression of a collagen adhesin is necessary and sufficient to mediate the attachment of Staphylococcus aureus to collagen-containing substrate. The ligand binding site within the 135-kDa S. aureus collagen adhesin and the collagen binding domain (CBD) was localized to a 168 amino acid long segment [CBD (151-318)] within the N-terminal portion of the adhesin. Short truncations in the terminal flanking regions of CBD (151-318) resulted in two CBS (180-318 and 151-297) that lacked collagen-binding activity.

Symersky et al Nat.Struct. Biol. 1997 Oct; 4(10): 833-8 teach the crystal structure of the recombinant 19,000 M(r) binding domain from the Staphylococcus aureus collagen adhesin. The domain fold is composed of two ant parallel beta-sheets and two short alpha helices. Triple-helical collagen model probes were used in a systematic docking search to identify the collagen-binding site. A groove on beta-sheet I exhibited the best surface complementarity to the collagen probes. This site partially overlaps with the peptide sequence previously shown to be critical for collagen binding. Recombinant proteins containing single amino acid mutations designed to disrupt the surface of the putative binding site exhibited significantly lower affinities for collagen.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this

Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D

NITA MINNIFIELD
PRIMARY EXAMINER
8/8/05